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=> d his

     (FILE 'HOME' ENTERED AT 13:33:24 ON 09 JAN 2002)

     FILE 'USPATFULL' ENTERED AT 13:40:16 ON 09 JAN 2002
L1             5 S ((SHARK CARTILAGE) (2A) EXTRACT)/CLM
L2             1 S ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W)HYPERTENS? OR AN
L3             2 S (SHARK CARTILAGE) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENSIVE
L4             1 S L3 NOT L2

     FILE 'CAPLUS' ENTERED AT 13:54:01 ON 09 JAN 2002
L5             1 S L2

     FILE 'WPIDS' ENTERED AT 13:55:00 ON 09 JAN 2002
L6             1 S L2
L7             5 S (ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENS

     FILE 'CAPLUS' ENTERED AT 14:06:52 ON 09 JAN 2002
L8             2 S (ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENS

     FILE 'USPATFULL' ENTERED AT 14:07:50 ON 09 JAN 2002
L9             0 S ((ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTEN
L10           12 S ((ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTEN
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Trying 3106016892...Open

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS 10	Aug 23	In-process records and more frequent updates now in MEDLINE
NEWS 11	Aug 23	PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS 12	Aug 23	Adis Newsletters (ADISNEWS) now available on STN
NEWS 13	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS 14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17	Oct 22	Over 1 million reactions added to CASREACT
NEWS 18	Oct 22	DGENE GETSIM has been improved
NEWS 19	Oct 29	AAASD no longer available
NEWS 20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS 22	Nov 29	COPPERLIT now available on STN
NEWS 23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS 24	Nov 30	Files VETU and VETB to have open access
NEWS 25	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 26	Dec 10	DGENE BLAST Homology Search
NEWS 27	Dec 17	WELDASEARCH now available on STN
NEWS 28	Dec 17	STANDARDS now available on STN
NEWS 29	Dec 17	New fields for DPCI
NEWS 30	Dec 19	CAS Roles modified
NEWS 31	Dec 19	1907-1946 data and page images added to CA and CAplus

NEWS EXPRESS	August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:33:24 ON 09 JAN 2002

=> file uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.80	1.80

FILE 'USPATFULL' ENTERED AT 13:40:16 ON 09 JAN 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 8 Jan 2002 (20020108/PD)
FILE LAST UPDATED: 8 Jan 2002 (20020108/ED)
HIGHEST GRANTED PATENT NUMBER: US6338160
HIGHEST APPLICATION PUBLICATION NUMBER: US2001047529
CA INDEXING IS CURRENT THROUGH 8 Jan 2002 (20020108/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 8 Jan 2002 (20020108/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2001
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2001

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s ((shark cartilage) (2a) extract)/clm
```
           164 SHARK/CLM
            24 SHARKS/CLM
           177 SHARK/CLM
                 ((SHARK OR SHARKS)/CLM)
           700 CARTILAGE/CLM
            24 CARTILAGES/CLM
           715 CARTILAGE/CLM
                 ((CARTILAGE OR CARTILAGES)/CLM)
            14 SHARK CARTILAGE/CLM
                 ((SHARK(W)CARTILAGE)/CLM)
         14613 EXTRACT/CLM
          3768 EXTRACTS/CLM
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         17451 EXTRACT/CLM
                 ((EXTRACT OR EXTRACTS)/CLM)
L1           5 ((SHARK CARTILAGE) (2A) EXTRACT)/CLM

=> d bib,kwic 1-5

L1   ANSWER 1 OF 5  USPATFULL
AN     2000:21612  USPATFULL
TI     Methods of using extracts of shark cartilage
IN     Dupont, Eric, St. Nicholas, Canada
       Brazeau, Paul, Montreal, Canada
       Juneau, Christina, Ste. Foy, Canada
       Maes, Daniel H., Huntington, NY, United States
       Marenus, Kenneth, Dix Hills, NY, United States
PA     Les Laboratoires Aeterna Inc., Quebec, Canada (non-U.S. corporation)
PI     US 6028118              20000222
AI     US 1996-693535          19960808 (8)
DT     Utility
FS     Granted
EXNAM  Primary Examiner: Eisenschenk, Frank C.; Assistant Examiner: Nelson,
       Brett
LREP   Matos, RickAkin, Gump, Strauss, Hauer & Feld, L.L.P.
CLMN   Number of Claims: 12
ECL    Exemplary Claim: 1
DRWN   31 Drawing Figure(s); 26 Drawing Page(s)
LN.CNT 2317
CLM    What is claimed is:
 . . . to transepidermal water loss, said method comprising the step of
       applying to the skin a therapeutically effective amount of a
       shark cartilage extract obtained by a
       process comprising the steps of: a) homogenizing shark cartilage in an
       aqueous solution in conditions which are. . .
 . . . soothing irritated mammalian skin, said method comprising the step of
       applying to the skin a therapeutically effective amount of a
       shark cartilage extract obtained by a
       process comprising the steps of: a) homogenizing shark cartilage in an
       aqueous solution in conditions which are. . .
 . . . inflammation in mammalian skin, said method comprising the step of
       applying to the skin a therapeutically effective amount of a
       shark cartilage extract obtained by a
       process comprising the steps of: a) homogenizing shark cartilage in an
       aqueous solution in conditions which are. . .
 . . . activity in mammalian skin, said method comprising the step of
       applying to the skin a therapeutically effective amount of a
       shark cartilage extract obtained by a
       process comprising the steps of: a) homogenizing shark cartilage in an
       aqueous solution in conditions which are. . .
 . . . atrophy in mammalian skin, said method comprising the step of
       applying to the skin a therapeutically effective amount of a
       shark cartilage extract obtained by a
       process comprising the steps of: a) homogenizing shark cartilage in an
       aqueous solution in conditions which are. . .
 . . . acne in mammalian skin, said method comprising the step of applying
       to the skin a therapeutically effective amount of a shark
       cartilage extract obtained by a process comprising the
       steps of: a) homogenizing shark cartilage in an aqueous solution in
       conditions which are. . .
 . . . psoriasis in mammalian skin, said method comprising the step of
       applying to the skin a therapeutically effective amount of a
       shark cartilage extract obtained by a
       process comprising the steps of: a) homogenizing shark cartilage in an
       aqueous solution in conditions which are. . .
```

. . . aging in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .

. . . eczema in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .

L1 ANSWER 2 OF 5 USPATFULL
AN 2000:18419 USPATFULL
TI Extracts of shark cartilage having anti-collagenolytic, anti-inflammatory, anti-angiogenic and anti-tumoral activities; process of making, methods of using and compositions thereof
IN Dupont, Eric, St. Nicolas, Canada
Brazeau, Paul, Montreal, Canada
Juneau, Christina, Ste. Foy, Canada
Maes, Daniel H., Huntington, NY, United States
Marenus, Kenneth, Dix Hills, NY, United States
PA Les Laboratoires Aeterna Inc., Canada (non-U.S. corporation)
PI US 6025334 20000215
AI US 1995-550003 19951030 (8)
RLI Continuation-in-part of Ser. No. US 1995-384555, filed on 3 Feb 1995, now patented, Pat. No. US 5618925, issued on 8 Apr 1997 which is a continuation-in-part of Ser. No. US 1994-234019, filed on 28 Apr 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Mohamed, Abdel A.
LREP Matos, RickAkin, Gump, Strauss, Hauer & Feld, L.L.P.
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 31 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 1732
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:

. . . of tumor proliferation, angiogenesis, inflammation and collagenolysis, the topical formulation comprising a pharmaceutical composition comprising an effective amount of a **shark cartilage extract** and an antioxidant, said **shark cartilage extract** being prepared according to a process comprising the steps of: a) homogenizing the cartilage in an aqueous solution in conditions. . .

. . . the method comprising the step of administering to a patient in need of such treatment an effective amount of a **shark cartilage extract**, said **shark cartilage extract** being prepared according to a process which comprises the following steps: a) homogenizing the cartilage in an aqueous solution in. . .

L1 ANSWER 3 OF 5 USPATFULL
AN 1999:146538 USPATFULL
TI Extracts of shark cartilage having an anti-angiogenic activity and an effect on tumor regression: process of making thereof
IN Dupont, Eric, St. Nicolas, Canada
Brazeau, Paul, Montreal, Canada
Juneau, Christian, Ste. Foy, Canada
PA Les Laboratories Aeterna Inc., Quebec, Canada (non-U.S. corporation)
PI US 5985839 19991116

AI US 1996-727300 19961008 (8)
RLI Continuation of Ser. No. US 1995-384555, filed on 3 Feb 1995, now patented, Pat. No. US 5618925 which is a continuation-in-part of Ser. No. US 1994-234019, filed on 28 Apr 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia; Assistant Examiner: Mohamed, Abdel A.
LREP Matos, RickAkin, Gump, Strauss, Hauer & Feld, L.L.P.
CLMN Number of Claims: 57
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1282
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
51. A **shark cartilage extract** comprising at least one biologically active component having a molecular weight of less than about 500 KDa; an anti-angiogenic activity;. . .
52. A **shark cartilage extract** according to claim 51, wherein said at least one biologically active component has a molecular weight in the range of. . .
53. A **shark cartilage extract** according to claim 51, wherein said at least one biologically active component comprises at least one biologically active component having. . .
54. A **shark cartilage extract** according to claim 51, wherein said at least at one biologically active component comprises at least one biologically active component. . .
55. A pharmaceutical composition comprising a **shark cartilage extract** as defined in claim 51.

. . . said method comprising the step of administering to a patient in need of such treatment an effective amount of a **shark cartilage extract** as defined in claim 51 for a period of time to sufficient treat said diseases or disorders.

L1 ANSWER 4 OF 5 USPATFULL
AN 97:29579 USPATFULL
TI Extracts of shark cartilage having an anti-angiogenic activity and an effect on tumor regression; process of making thereof
IN Dupont, Eric, St. Nicolas, Canada
Brazeau, Paul, Montreal, Canada
Juneau, Christi, Ste. Foy, Canada
PA Les Laboratories Aeterna Inc., Quebec, Canada (non-U.S. corporation)
PI US 5618925 19970408
AI US 1995-384555 19950203 (8)
RLI Continuation-in-part of Ser. No. US 1994-234019, filed on 28 Apr 1994
DT Utility
FS Granted
EXNAM Primary Examiner: Weimar, Elizabeth C.; Assistant Examiner: Mohamed, Abdel A.
LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1153
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
1. A process for obtaining a solid **extract** of **shark cartilage** having anti-angiogenic, direct anti-tumoral and anti-tumor proliferating activities, which comprises the following steps: a) homogenizing pieces of solid shark cartilage. . .
7. A process for obtaining a liquid **extract** of **shark**

cartilage which comprises the following steps: a) homogenizing pieces of solid shark cartilage in a non-denaturing aqueous solution until said pieces. . .
26. A process for obtaining a liquid **extract** of **shark cartilage** having anti-angiogenic, direct anti-tumoral and anti-tumor proliferating activities which comprises the following steps, all performed at about 4.degree. C.: a). . .

L1 ANSWER 5 OF 5 USPATFULL
AN 84:53979 USPATFULL
TI Anti-inflammatory composition
IN Schinitsky, Michael, Madison, WI, United States
PA Faxon Pharmaceuticals, Inc., Madison, WI, United States (U.S. corporation)
PI US 4473551 19840925
AI US 1983-502716 19830609 (6)
RLI Continuation-in-part of Ser. No. US 1982-410447, filed on 23 Aug 1982, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Rosen, Sam
LREP Barnes & Thornburg
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 344
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
. . . 10 wherein said cartilage is administered in the form of the greater than 100,000 molecular weight fraction of an aqueous **extract** of whole **shark cartilage**.

=> d pn 1-5

L1 ANSWER 1 OF 5 USPATFULL
PI US 6028118 20000222

L1 ANSWER 2 OF 5 USPATFULL
PI US 6025334 20000215

L1 ANSWER 3 OF 5 USPATFULL
PI US 5985839 19991116

L1 ANSWER 4 OF 5 USPATFULL
PI US 5618925 19970408

L1 ANSWER 5 OF 5 USPATFULL
PI US 4473551 19840925

=> d ai 1-5

L1 ANSWER 1 OF 5 USPATFULL
AI US 1996-693535 19960808 (8)

L1 ANSWER 2 OF 5 USPATFULL
AI US 1995-550003 19951030 (8)

L1 ANSWER 3 OF 5 USPATFULL
AI US 1996-727300 19961008 (8)

L1 ANSWER 4 OF 5 USPATFULL
AI US 1995-384555 19950203 (8)

L1 ANSWER 5 OF 5 USPATFULL
AI US 1983-502716 19830609 (6)

=> s ((shark cartilage) (2a) extract) and (anti(w)hypertens? or antihypertensive or ((Calcium or Ca) (2w) blocker#) or verapamil or nifedipin or diltiasem)

```
          1189 SHARK
           351 SHARKS
          1407 SHARK
                 (SHARK OR SHARKS)
          6873 CARTILAGE
           447 CARTILAGES
          7064 CARTILAGE
                 (CARTILAGE OR CARTILAGES)
            88 SHARK CARTILAGE
                 (SHARK(W)CARTILAGE)
        143384 EXTRACT
         95409 EXTRACTS
        191564 EXTRACT
                 (EXTRACT OR EXTRACTS)
             9 (SHARK CARTILAGE) (2A) EXTRACT
        220674 ANTI
            19 ANTIS
        220683 ANTI
                 (ANTI OR ANTIS)
         16378 HYPERTENS?
          2456 ANTI(W)HYPERTENS?
          5646 ANTIHYPERTENSIVE
          1789 ANTIHYPERTENSIVES
          6689 ANTIHYPERTENSIVE
                 (ANTIHYPERTENSIVE OR ANTIHYPERTENSIVES)
        215896 CALCIUM
            54 CALCIUMS
        215898 CALCIUM
                 (CALCIUM OR CALCIUMS)
        111832 CA
         12083 CAS
        121951 CA
                 (CA OR CAS)
         10010 BLOCKER#
          2056 (CALCIUM OR CA) (2W) BLOCKER#
          1928 VERAPAMIL
             3 VERAPAMILS
          1928 VERAPAMIL
                 (VERAPAMIL OR VERAPAMILS)
            82 NIFEDIPIN
             2 DILTIASEM
L2           1 ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W)HYPERTENS? OR ANTIH
               YPERTENSIVE OR ((CALCIUM OR CA) (2W) BLOCKER#) OR VERAPAMIL OR
               NIFEDIPIN OR DILTIASEM)
```

=> d kwic

L2 ANSWER 1 OF 1 USPATFULL
DETD . . . compounds that interfere with DNA replication, mitosis and chromosomal segregation. Such chemotherapeutic compounds include adriamycin, also known as doxorubicin, etoposide, **verapamil**, podophyllotoxin, and the like. Widely used in a clinical setting for the

treatment of neoplasms, these compounds are administered through. . .

DETD CAI is a small molecular weight synthetic inhibitor of angiogenesis that acts as a **calcium** channel **blocker** that prevents actin reorganization, endothelial cell migration and spreading on collagen IV. CAI inhibits neovascularization at physiological attainable concentrations and. . .

DETD . . . acids and paclitaxel (U.S. Pat. No. 5,716,981; incorporated herein by reference); AGM-1470 (Ingber el al., 1990; incorporated herein by reference); **shark cartilage extract** (U.S. Pat. No. 5,618,925; incorporated herein by reference); anionic polyamide or polyurea oligomers (U.S. Pat. No. 5,593,664; incorporated herein by. . .

=> d hit

L2 ANSWER 1 OF 1 USPATFULL

DETD Further useful agents include compounds that interfere with DNA replication, mitosis and chromosomal segregation. Such chemotherapeutic compounds include adriamycin, also known as doxorubicin, etoposide, **verapamil**, podophyllotoxin, and the like. Widely used in a clinical setting for the treatment of neoplasms, these compounds are administered through bolus injections intravenously at doses ranging from 25-75 mg/m.sup.2 at 21 day intervals for adriamycin, to 35-50 mg/m.sup.2 for etoposide intravenously or double the intravenous dose orally.

DETD CAI is a small molecular weight synthetic inhibitor of angiogenesis that acts as a **calcium** channel **blocker** that prevents actin reorganization, endothelial cell migration and spreading on collagen IV. CAI inhibits neovascularization at physiological attainable concentrations and is well tolerated orally by cancer patients. Clinical trials with CAI have yielded disease stabilization in 49% of cancer patients having progressive disease before treatment.

DETD Further specific angiogenesis inhibitors, including, but not limited to, Anti-Invasive Factor, retinoic acids and paclitaxel (U.S. Pat. No. 5,716,981; incorporated herein by reference); AGM-1470 (Ingber el al., 1990; incorporated herein by reference); **shark cartilage extract** (U.S. Pat. No. 5,618,925; incorporated herein by reference); anionic polyamide or polyurea oligomers (U.S. Pat. No. 5,593,664; incorporated herein by reference); oxindole derivatives (U.S. Pat. No. 5,576,330; incorporated herein by reference); estradiol derivatives (U.S. Pat. No. 5,504,074; incorporated herein by reference); and thiazolopyrimidine derivatives (U.S. Pat. No. 5,599,813; incorporated herein by reference) are also contemplated for use as anti-angiogenic compositions for the combined uses of the present invention.

=> d

L2 ANSWER 1 OF 1 USPATFULL

AN 2001:196603 USPATFULL

TI Cancer treatment methods using therapeutic conjugates that bind to aminophospholipids

IN Thorpe, Philip E., Dallas, TX, United States
Ran, Sophia, Dallas, TX, United States

PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)

PI US 6312694 B1 20011106

AI US 1999-351457 19990712 (9)

PRAI US 1998-92589 19980713 (60)
US 1998-110600 19981202 (60)

```
DT      Utility
FS      GRANTED
LN.CNT 8243
INCL    INCLM: 424/178.100
        INCLS: 424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100;
               424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100;
               514/012.000; 530/387.100; 530/388.100
NCL     NCLM:  424/178.100
        NCLS:  424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100;
               424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100;
               514/012.000; 530/387.100; 530/388.100
IC      [7]
        ICM: A61K039-395
        ICS: C12P021-08; C07K016-00
EXF     514/12; 424/133.1; 424/135.1; 424/136.1; 424/137.1; 424/141.1;
        424/142.1; 424/143.1; 424/178.1; 424/181.1; 424/193.1; 530/387.1;
        530/388.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> s (shark cartilage) and (anti(w)hypertens? or antihypertensive or ((Calcium or
Ca) (2w) blocker#) or verapamil or nifedipin or diltiasem)
          1189 SHARK
           351 SHARKS
          1407 SHARK
                 (SHARK OR SHARKS)
          6873 CARTILAGE
           447 CARTILAGES
          7064 CARTILAGE
                 (CARTILAGE OR CARTILAGES)
            88 SHARK CARTILAGE
                 (SHARK(W)CARTILAGE)
        220674 ANTI
            19 ANTIS
        220683 ANTI
                 (ANTI OR ANTIS)
         16378 HYPERTENS?
          2456 ANTI(W)HYPERTENS?
          5646 ANTIHYPERTENSIVE
          1789 ANTIHYPERTENSIVES
          6689 ANTIHYPERTENSIVE
                 (ANTIHYPERTENSIVE OR ANTIHYPERTENSIVES)
        215896 CALCIUM
            54 CALCIUMS
        215898 CALCIUM
                 (CALCIUM OR CALCIUMS)
        111832 CA
         12083 CAS
        121951 CA
                 (CA OR CAS)
         10010 BLOCKER#
          2056 (CALCIUM OR CA) (2W) BLOCKER#
          1928 VERAPAMIL
             3 VERAPAMILS
          1928 VERAPAMIL
                 (VERAPAMIL OR VERAPAMILS)
            82 NIFEDIPIN
             2 DILTIASEM
L3           2 (SHARK CARTILAGE) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENSIVE OR
               ((CALCIUM OR CA) (2W) BLOCKER#) OR VERAPAMIL OR NIFEDIPIN OR
               DILTIASEM)
```

=> s l3 not l2
L4 1 L3 NOT L2

=> d bib,hit

L4 ANSWER 1 OF 1 USPATFULL
AN 2001:182585 USPATFULL
TI Compositions and methods for prevention and treatment of chronic diseases and disorders including the complications of diabetes mellitus
IN Kosbab, John V., Dillon, CO, United States
PI US 2001031744 A1 20011018
AI US 2001-827251 A1 20010405 (9)
RLI Continuation of Ser. No. US 1998-18273, filed on 4 Feb 1998, ABANDONED
PRAI US 1997-37084 19970204 (60)
US 1997-43262 19970417 (60)
DT Utility
FS APPLICATION
LREP GREENLEE WINNER and SULLIVAN, P.C., Suite 201, 5370 Manhattan Circle, Boulder, CO, 80303
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2318
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0024] (iv) A neovascular regulator selected from genistein and/or daidzein; soy isolate comprising genistein and/or daidzein; cartilage or chondroitin sulphate; chondroitin sulphate is a preferred neovascular regulator also associated with collagen synthesis; **shark cartilage** is a preferred cartilage preparation.

SUMM [0211] A source of cartilage or a cartilage preparation, e.g., **shark cartilage**.

SUMM [0235] (iii) A neovascular regulator selected from genistein and/or diadzein; soy isolate comprising genistein and/or diadzein; **shark cartilage** or chondroitin sulphate.

SUMM [0245] Glucosamine sulphate; and optionally a cartilage preparation, e.g., **shark cartilage**

SUMM [0372] One or more of the functionalities listed in Table 1 can be provided in the compositions of this invention by art-known drug equivalents. For example, art-known antidiabetic agents, **antihypertensives**, angiotensin converting enzyme inhibitors, vasodilators, anticholesteremics, antihyperlipoproteinemics, angiogenesis regulators, and enzyme co-factors can be combined in effective amounts for ameliorating symptoms and conditions associated with microangiopathy, particularly retinopathy and nephropathy, with formulas of this invention.

SUMM [0406] Green tea extract, tea polyphenols, contains a small amount of 2-3% of proanthocyanidin. It nevertheless is a potent antioxidant for lipid peroxides, superoxides and hydroxyl radicals. It contains relatively high concentrations of (-) epigallocatechin gallate (EGCg), a condensed tannin polyphenol. In addition to antioxidant function, tea polyphenols also have anti-platelet, anti-cholesterolemia, **anti-hypertension**, anti-hyperglycemic and anti-mutagenic activities. Tea polyphenols also assist theoflavin digallate in acting as an angiotensin converting enzyme inhibitor, but do not have the undesired pro-oxidant properties of captopril.

SUMM [0411] Cartilage, an avascular tissue, is a source of angiogenesis

inhibitor(s). Shark and bovine cartilage, among others, are sources of angiogenesis inhibitor and may provide collagenase inhibition as well. Chondroitin sulphate, a mucoploysaccharide found in most mammalian cartilaginous tissues and **shark cartilage**, is believed by many to be the most active angiogenesis regulating component of **Shark Cartilage**. The restoration of diabetic depleted chondroitin sulphates may also affect collagen stabilization which would help to normalize the collagen matrix of vascular tissue and therefore create a more stable vascular structure. Chondroitin sulphate can be provided in a number of forms with different counterions, e.g., sodium, potassium, etc. Sodium chondroitin sulphate is the form preferred for use in compositions of this invention.

SUMM [0414] Heparin sulphate levels are increased in diabetics while levels of chondroitin sulphates are decreased. This suggests an imbalance in chondroitin sulphate and in angiogenic regulation. Gymnema Sylvestre which normalizes heparin levels is provided in the compositions of this invention, at least in part, to affect heparin levels which in turn may affect angiogenic regulation due to **shark cartilage** and protamine sulfate which both bind to heparin. The insulin/glucose stabilization effects of Gymnema sylvestre would reduce the oxidative stress that contributes to the neovascularization factors described above.

SUMM [0457] Gymnemic acid, the active ingredient in Gymnema sylvestre, suppresses sensitivity to sugar and its absorption, thereby reducing blood glucose levels. It also restores the levels of three chondroitin sulfates which may assist in collagen repair and/or aid in angiogenesis regulation. Heparin sulphate levels are increased in diabetics while three chondroitin sulfates are decreased. Gymnema sylvestre which normalizes heparin levels could play a supporting role in the angiogenic regulation of other ingredients in this formulation, namely **shark cartilage** and protamine sulfate. Both are angiogenic regulators which bind to heparin. The restoration of depleted chondroitin sulfates probably plays a role in collagen stabilization which would help to normalize the collagen matrix and therefore create a more stable structure upon which angiogenesis regulation could more easily exist. The insulin/glucose stabilization effects of Gymnema sylvestre would reduce the oxidative stress that contributes to the neovascularization factors described above.

DETD [0496] **Shark cartilage** powder (100%, 200 mesh) was obtained from Global Trading (USA) Inc. (Union, N.J.).

DETD [0503] Those of ordinary skill in the art of formulation of nutrients and therapeutic compositions will appreciate that components functionally equivalent to those specifically disclosed herein, as well as alternative forms and sources in addition to those specifically disclosed herein for individual composition ingredients are available. This invention is intended to encompass all such functional equivalents and alternatives that are readily known to the art.

TABLE 1

Summary of Functions of Components of Compositions of this invention for Microangiopathy and Macroangiopathy

Primary formulas comprise components which:

1. Function as antioxidant to control oxidative stress;
2. Function as neovascular regulators controlling angiogenesis to promote vascular healing and integrity;
3. Stabilize glucose and amylase factors, for example, to increase

glucose tolerance in diabetes; and

4. Supplement dietary deficiencies and loss through spillage, particularly as associated with diabetes.

Compositions of this invention can further comprise components which:

5. Stabilize insulin supply and decrease sensitivity to glucose;
6. Stabilize protein factors, control proteinuria, glycosylation and albumin;
7. Control anti-sclerotic factors, functioning as/to:
   A. Anti-platelet or anti-thrombic agents
   B. Homocysteine inhibitors
   C. Reduce atherosclerotic lesions
   D. Reduce LDL and VLDL
   E. Improve HDL/LDL ratio
   F. Inhibit lipoprotein (a) production
   G. Inhibit cholesterol absorption in bowel
   H. Enhance cholesterol excretion
   I. Triglycerides inhibitors
   J. Fibrogen inhibitors
   K. Nitric Oxide inhibitors (Optional)
   L. Ketosis regulators
8. Reduce immune phagocytic response to:
   A. Leukotrienes, neutrophils, etc.
   B. Immunoglobulin (a)
9. Reduce and stabilize **anti-hypertensives** as:
   A. Angiotensin converting enzyme inhibitors & vasodilators
   B. Prostacyclin inhibitors
   C. Aldose Reductase inhibitors
   D. Blood pressure inhibitor/regulator (systolic only)
   E. Agents to reduce blood pressure during bowel contractions
   F. Anti-edema agent
   G. Histamine suppressors
10. Enhance cellular or metabolic function, for example for:
   A. Glutathione restoration
   B. ATP/NAD restoration
11. Promote vascular healing and integrity by:
   A. Restoring the collagen matrix
   B. Histamine suppression (Optional)
12. Promote better nutrient digestion and absorption
13. Improve pH factor by controlling digistens and systemic hyperacidity
14. Participate in collagen synthesis
15. Calcium regulator
16. Control myocardial infarction and damage
17. Increase cardiovascular exercise ability and tolerance
18. Increase other antioxidants, including Vitamin E, reduced glutathione, uric acid, superoxide dismutase (SOD), catalyze, or glutathione peroxidase
19. Inhibit breakdown of myocardial cell membrane
20. Provide immune differentiation
21. Restore Vitamin E levels by intestinal absorption of omega-3-fatty acids
22. Improves cell transport and mitochondrial function
23. Improves sleep for better disease resistance and recovery
24. Amino acid believed to inhibit or ameliorate diabetes pathogenesis
25. Amino acid believed to inhibit or ameliorate cardiovascular pathogenesis
26. Amino acid believed to contribute to wound healing or prevention
27. Amino acid believed to inhibit or ameliorate neuropathic pathogenesis
28. Amino acid believed to inhibit or ameliorate dental and periodontal pathogenesis
29. Promoter of DNA polymerase for wound healing
30. Provides protein sources for wound healing
31. Contributes to improved bone density

32. Promotes anti-caries and anti-gingivitis environment
33. Accelerates wound healing
DETD [0506]
TABLE 4

Exemplary Diabetic Compliations Formulation Dosages

COMPONENT	AVERAGE ADULT DOSE PER DAY - mg/day FORMULATION A	AVERAGE ADULT DOSE PER DAY - mg/day FORMULATION B
Bilberry Extract, 25% OPC	375	375
Calcium (Krebs)	500 (110 active)	500 (110 active)
Chondroitin Sulfate	750	750
Chromium Picolinate	200 .mu.g (24.60 .mu.g active)	200 .mu.g (24.60 .mu.g active)
CoQ10	20	20
Fenugreek Seed Powder	150	150
Flax Seed Powder	500	500
Folic Acid	800 .mu.g	450 .mu.g
Linoleic Acid	25	25
Ginko Biloba 24%	25	25
Gymnema Sylvestre	250	250
Taurine or Homotaurine	100	100
Grape Seed extract, 95-100% OPC	100	100
Acetyl-l-carnitine	50	50
Lutein	120	120
Magnesium (Krebs)	300 (48 active)	300 (48 active)
N-Acetyl-l-cysteine	200	200
Pine Bark Extract (greater than 85% OPC)	20	20
Phytosterol Complex (Cholestatin III)	200	200
Potassium Citrate	90 (32.4)	90 (32.4)
Protamine Sulfate	50	50
Shark Cartilage 100%	1,000	1,000
Soy Isolate	1,000 (920 active)	1,000 (920 active)
Green Tea Polyphenols	100	100
Lipoic Acid	20	20
Vitamin A (Acetate Formula A) (Palmitate Formula B)	5,000 iu	5,000 iu
Vitamin B-2 (Riboflavin)	3	50
Vitamin B-6 (Pyridoxine hydrochloride)	4.88 active (4.0 active)	213.4 (175 active)
Vitamin B-12 (Cyanocobalamin 1%)	100 .mu.g active	100 .mu.g active
Vitamin C (Ascorbic acid)	1,000	1,000
Vitamin E, d-alpha tocopheryl acetate	714 (500 iu active)	714 (500 iu active)
Zinc (Krebs)	30 (9 active)	30 (9 active)

```
=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                        42.22      44.02

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FILE COVERS 1907 - 9 Jan 2002  VOL 136 ISS 2
FILE LAST UPDATED: 7 Jan 2002  (20020107/ED)

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=> d his

     (FILE 'HOME' ENTERED AT 13:33:24 ON 09 JAN 2002)

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L2             1 S ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W)HYPERTENS? OR AN
L3             2 S (SHARK CARTILAGE) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENSIVE
L4             1 S L3 NOT L2

     FILE 'CAPLUS' ENTERED AT 13:54:01 ON 09 JAN 2002

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          3338 SHARK
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          17628 CARTILAGE
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                  (SHARK(W)CARTILAGE)
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          28628 EXTRACTS
          49577 EXTRACT
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         188279 EXTS
         397312 EXT
                  (EXT OR EXTS)
         410797 EXTRACT
                  (EXTRACT OR EXT)
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              7 ANTIS
         261327 ANTI
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            396 ANTI(W)HYPERTENS?
          21019 ANTIHYPERTENSIVE
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              1 DILTIASEM
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                NIFEDIPIN OR DILTIASEM)

=> d bib,kwic

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   1999:64822  CAPLUS
DN   130:90515
TI   A preparation derived from shark cartilage for treatment of diseases
     related to excessive parathyroid hypertensive factor or excessive
     intracellular calcium
IN   Pang, Peter K. T.; Shan, Jacqueline J.; Chiu, Kam W.
PA   CV Technologies Inc., Can.
SO   PCT Int. Appl., 30 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	EP 1012163	A1	20000628	EP 1998-934212	19980709
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	JP 2001509513	T2	20010724	JP 2000-502067	19980709
PRAI	US 1997-52233	P	19970711		
	WO 1998-US13591	W	19980709		

RE.CNT 6

RE

(1) Dupont; US 5618925 A 1997 CAPLUS
(2) Furuhashi; US 3371012 A 1968
(3) Lane; US 5075112 A 1991
(4) Pang; US 5192664 A 1993 CAPLUS
(6) Schinitsky; US 4473551 A 1984 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB **Shark cartilage ext.** has been shown to be an antagonist of parathyroid hypertensive factor (PHF). In view of this, **shark cartilage ext.** can be used to treat conditions related to excessive PHF activity. Such diseases include hypertension and some other diseases related to intracellular calcium elevation. Methods for producing the **shark cartilage ext.** and methods for administering the ext. are disclosed.

ST **shark cartilage ext** parathyroid hypertensive factor inhibition hypotensive; calcium disease **shark cartilage ext** parathyroid hypertensive factor inhibition

IT Mucopolysaccharides, biological studies
Proteins (general), biological studies
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(in **shark cartilage ext.**; **shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT Vascular smooth muscle
(proliferation inhibition; **shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT **Antihypertensives**
Cartilage
Drug delivery systems
Shark
(**shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT Antiproliferative agents
(vascular smooth muscle; **shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT 25322-46-7, Chondroitin sulfate C
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(in **shark cartilage ext.**; **shark**

cartilage ext. for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT 7440-70-2, Calcium, biological studies 130037-95-5, Parathyroid hypertensive factor
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

=> file wpids

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	22.49	66.51
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.62	-0.62

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FILE LAST UPDATED: 05 JAN 2002 <20020105/UP>
MOST RECENT DERWENT UPDATE 200201 <200201/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

=> s l2

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            9 ANTIS
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             1 DILTIASEM
L6           1 ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W)HYPERTENS? OR ANTIH
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               NIFEDIPIN OR DILTIASEM)

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L6   ANSWER 1 OF 1  WPIDS COPYRIGHT 2002   DERWENT INFORMATION LTD
AN   1999-120772 [10]   WPIDS
DNC  C1999-035371
TI   Shark cartilage extract - has
     anti-parathyroid hypertensive factor activity.
DC   B04
IN   CHIU, K W; PANG, P K T; SHAN, J J
PA   (CVTE-N) CV TECHNOLOGIES INC
CYC  83
PI   WO 9902548    A1 19990121 (199910)* EN   29p    C07K001-00
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            OA PT SD SE SZ UG ZW
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     CN 1263534    A  20000816 (200055)              C07K001-00
     JP 2001509513 W  20010724 (200147)       32p    A61K035-32
     KR 2001021764 A  20010315 (200159)              C07K001-00
ADT  WO 9902548 A1 WO 1998-US13591 19980709; AU 9883790 A AU 1998-83790
     19980709; EP 1012163 A1 EP 1998-934212 19980709, WO 1998-US13591 19980709;
     CN 1263534 A CN 1998-807088 19980709; JP 2001509513 W WO 1998-US13591
     19980709, JP 2000-502067 19980709; KR 2001021764 A KR 2000-700327 20000111
FDT  AU 9883790 A Based on WO 9902548; EP 1012163 A1 Based on WO 9902548; JP
     2001509513 W Based on WO 9902548
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          A61P043-00; C07K001-02
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